DETAILED ACTION

Applicant's election **without** traverse dated October 10, 2008 is acknowledged. Applicants have elected the invention of group I comprising claims 1-5, 10-12 and 16. Claims 6-9, 13-15 and 17-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected groups, there being no allowable or linking claims.

Although the elected group was made without traverse, the response includes the following argument:

"Although examination is currently restricted to an isolated polynucleotide comprising a nucleic acid sequence encoding geraniol synthase, an expression vector and prokaryotic organism comprising the nucleic acid sequence encoding geraniol synthase and a method for producing recombinant geraniol synthase, Applicants request that the method for producing geraniol embodied in claims 13-15 and the use of geraniol or metabolites thereof embodied in claims 17and 18 be rejoined into the application to the extent that such claims have the same limitations as any allowed expression vector of claim 10".

Applicant's argument has been considered. The method of using the product encompassed in claims 13-15 will be considered in the event that the invention in group I is found allowable. The invention of group IV comprises claims 17 and 18 and is drawn to the use of geraniol or metabolites in agricultural, cosmetic and food products. Inventions in group I and IV are unrelated these inventions are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the polynucleotide, vectors and host cells claimed in group I are not capable of being used together. Therefore group IV comprising claims 17 and 18 is withdrawn. Claims 1-5, 10-12 and 16 are present for examination.

Priority

Priority for this application which is a 371 of PCT/US04/40321 filed on 12/02/2004 is acknowledged for benefit of U.S. Provisional Application No. 60/528,202, filed on December 10, 2003.

Information Disclosure Statement

The information disclosure statement filed on June 09, 2006 has been considered as shown by the Examiners signature.

Oath/Declaration

The oath or declaration submitted on February 04, 2008 has been reviewed and is in compliance with 37 CFR 1.56.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below

In particular, of 37 CFR 1.821 (d), which states:

(d) Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence using the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

In the instant case, the requirements are not met because, this application, contains sequences, that were not assigned a sequence identifier number in fig. 1 and in fig. 2 (see sequence alignment comprising polypeptide sequences of 4S-lim and 1, 8-cin).

Drawings

The drawings in Fig. 2 is objected to under 37 CFR 1.83(a) because they fail to show the required details as described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). The drawings are objected to because the alignment in figure 2 does not clearly show the amino acids that are similar or identical. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "derivative" or "analogue" in claim 5, renders the claim(s) indefinite because the claim(s) include(s) elements not actually disclosed, thereby rendering the scope of the claim(s) unascertainable. See MPEP § 2173.05(d).

Based on the specification one of ordinary skill in the art cannot ascertain the identity of "derivatives" or "an analogues" of the polypeptide encoded by the polynucleotide of SEQ ID NO: 1. Clarification is required.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131

USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 4 recites the broad recitation at least 60%, and the claim also recites preferably at least 70%, more preferably at least 80% or more, most preferably at least 90% which are successively narrower statements of the range/limitation.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, 5, 10-12 and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Factors to be considered in making the determination as to whether one skilled in the art would recognize that the applicant was in possession of the claimed invention as a whole at the time of filing include: **a**. Actual reduction to practice; **b.** Disclosure of drawings or structural chemical formulas;

c. Sufficient relevant identifying characteristics such as

i. Complete structure,

ii. Partial structure,

iii. Physical and/or chemical properties or

iv. Functional characteristics when coupled with a known or disclosed correlation between function and structure;

d. Method of making the claimed invention; **e.** Level of skill and knowledge in the art and **f.** Predictability in the art.

While all of these factors are considered, a sufficient number for a *prima facie* case are discussed as they relate to the issues mentioned above.

Claims 1, 10-12 and 16 are directed to a genus of polynucleotide sequences encoding any geraniol synthase (GES) from any source, vectors comprising the same and host cells comprising said vectors with the only requirement that the GES encoded by said genus of polynucleotides have the ability to convert geranyl diphosphate to geraniol.

Furthermore claims 4 and 5 are directed to a genus of polynucleotide sequences that encode amino acid sequences that are 60-90% homologous to SEQ ID NO: 2 or are fragments, derivatives or analogs of SEQ ID NO: 2 with geraniol synthase activity i.e. that can convert geranyl diphosphate to geraniol (claims 4 and 5).

However the specification only discloses the reduction into practice of the polynucleotide sequence of SEQ ID NO: 1 that encodes the amino acid sequence of SEQ ID NO: 2 which has the ability to convert geranyl diphosphate to geraniol. Applicants have not reduced into practice the claimed genus of polynucleotide sequences that encode geraniol synthases having any structure, or that encode proteins with 60%-90% sequence identity to SEQ ID NO: 2 or fragments, derivatives and analogs thereof that retain GES activity. The specification refers to various ways of producing variants of SEQ ID NO: 1 and relies on teachings in the art for

methods of designing these variants (such as PCR and site directed mutagenesis). However the specification does not disclose even a single variant of SEQ ID NO: 1 that encodes a polypeptide with geraniol synthase activity. The specification does not describe where, in the polynucleotide sequence of SEQ ID NO: 1 the variation can be while preserving the activity of the encoded polypeptide. Applicants show an alignment between the basil geraniol synthetase encoded by SEQ ID NO 1 and two other terpene synthase sequences. However this alignment only shows two other terpene synthases that appear to have discrete regions of identity/similarity to the polypeptide encoded by SEQ ID NO: 1. Thus this sequence alignment does not put the skilled artisan in possession of the genus of polynucleotides encompassed in the claims.

The specification does not teach polynucleotide variants, with up to 40% variation or fragments, analogues and derivatives that retain geraniol synthase activity. The specification does not teach what the structure of polynucleotides that encode derivative and analogues of SEQ ID NO: 2 would look like or how these polynucleotides differ from their natural counterparts. Furthermore at the time the instant invention was disclosed there was no art recognized correlation between any structure (other that the polypeptide of SEQ ID NO: 2 encoded by SEQ ID NO: 1) and geraniol synthase activity. Thus one of skill in the art cannot predict which nucleotide residues within SEQ ID NO: 1 can be varied without disrupting the activity of the encoded protein. Therefore the specification lacks information regarding variants that retain geraniol synthase activity.

The level of skill in the art is such that one of skill would not be able to identify without further testing which of the genus of variant discussed above encode polypeptides that retain geraniol synthase activity. Based on the lack of knowledge and predictability in the art, those

skilled in the art would not conclude that applicants was in possession of the claimed genus of proteins based on disclosure of the polynucleotide of SEQ ID NO: 1.

Claims 1, 2, 4, 5, 10-12 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide of SEQ ID NO: 1 that encodes the polypeptide of SEQ ID NO: 2 with geraniol synthase activity (GES) does not reasonably provide enablement for any polynucleotide encoding polypeptide variants with 60%, 70%, 80% or 90% sequence identity to a polynucleotide encoding SEQ ID NO: 2 or fragments and derivatives or analogues of SEQ ID NO: 2 that retains GES activity. Furthermore the specification does not provide enablement on how to use the full scope of polynucleotides sequences of any size and level of identity that can hybridize under any hybridization condition with the polynucleotide of SEQ ID NO: 1 where said sequences encodes an amino acid sequence with or without enzymatic activity (claim 2(d)).

The specification does not enable any person skilled in the art to which it pertains to, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 1, 4, 5, 10-12 and 16 are so broad as to encompass any polynucleotide from any source with any sequence structure that encodes a polypeptide with geraniol synthase (GES) activity or any polynucleotide that encodes a polypeptide variant comprising 10%-40% compared to the sequence of SEQ ID NO: 2. Furthermore claim 5 encompasses any polynucleotide that encodes polypeptide fragments of any size, derivatives and analogues of SEQ ID NO: 2 that show GES activity. Claim 2(d) encompasses any polynucleotide of any size that can hybridize under

any condition to the polynucleotide of SEQ ID NO: 1 or its complement wherein said polynucleotide can encode a protein with or without enzymatic activity. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number polynucleotide sequences broadly encompassed by the claims.

The factors to be considered in determining whether undue experimentation is required are summarized ln re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988).

The Wands factors are: (1) nature of the invention, (2) state of the prior art, (3) relative skill of those in the art, (4) predictability or unpredictability of the art, (5) amount or direction or guidance presented, (6) presence or absence of working examples, (7) breadth of the claims and (8) quantity of experimentation necessary.

While all of these factors are considered, a sufficient number for *prima facie* case are discussed.

The nature of the invention encompasses an isolated polynucleotide, vector and host cells comprising said polynucleotide which encodes the geraniol synthase of SEQ ID NO: 2 which specifically catalyzes the conversion of geranyl diphosphate to geraniol. However as explained above the scope of the claims as broadly interpreted encompasses any polynucleotide that encodes any polypeptide with any structure or any fragment, derivative or analogue thereof ((claim 1, 2, 4, 5, 10-12 and 16)) with or without the ability to convert geranyl diphosphate to geraniol. However the specification only teaches none, except the polynucleotide of SEQ ID NO: 1 that encodes the amino acid sequence of SEQ ID NO: 2, vectors and host cells comprising the same that has the ability to catalyze the conversion of geranyl diphosphate to geraniol.

One of skill in the art gleaning at the specification would not be able to predict which nucleotide residues within SEQ ID NO: 1 can be varied without disrupting GES activity because the specification lacks information regarding the nucleic acid residues that can be varied within SEQ ID NO: 1 and encode polypeptide variants (of SEQ ID NO: 2) that still retain geraniol synthase activity.

The disclosure of a single polynucleotide would not allow a skilled artisan to predict the structure of the broad genus of polynucleotide sequences that encode polypeptides with 10%-40% variation relative to SEQ ID NO: 2 were all of these variants have GES activity.

Furthermore since there is not much known about variants of the polynucleotide sequence encoding geraniol synthase of SEQ ID NO: 2, the specification would need to have more detail as how to make and use the full scope of the invention.

The level of skill in the art is high because one of skill would not be unable to make or use any variant or a variant comprising 10%-40% changes or fragments of any size, derivatives and analogues of SEQ ID NO: 2 without further testing each variant for it's ability to catalyze the conversion of geranyl diphosphate to geraniol. Furthermore the specification is silent with regards to polynucleotides that encode derivatives and analogues of SEQ ID NO: 2 thus does not teach how to make and how to use such sequences.

The quantity of experimentation required to identify polynucleotides encoding polypeptide variants with the above degree of variations while retaining the desired activity is enormous. Furthermore claim 2 encompasses any polynucleotide sequence of any size that hybridizes with SEQ ID NO: 1 under any hybridization condition. Thus the scope of the polynucleotide sequences can encompasses any polynucleotide of any size with limited sequence

identity to SEQ ID NO: 1. Polynucleotide that hybridizes with SEQ ID NO: 1 can encode polypeptides with or with no enzymatic activity wherein the enzymatic activity is not limited to geraniol synthase activity. However the specification does not teach how to use the enormous scope encompassed in this claim. Thus the disclosure of the polynucleotide sequence of SEQ ID NO: 1 is insufficient to provide enablement for the enormous scope encompassed in the claims.

The Examiner finds that one skilled in the art would require additional guidance, such as information regarding the structure of polynucleotides variants that encode polypeptide fragments, derivatives or analogues that retain geraniol synthase activity. Such guidance includes a teaching with regards to the region(s) in the polynucleotide structure that if altered would not disrupt the activity of the encoded polypeptide. Furthermore such guidance includes a teaching of how to make polynucleotides that encode functional polypeptides derivatives and analogues of SEQ ID NO: 2. Without such guidance, the experimentation left to those skilled in the art is undue.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 2 is rejected under 35 U.S.C. 102(b) as being anticipated by US 6,559,2971 filed June 29, 2001 published to Chappell et al[1] or US 6,468,772 filed on September 14, 1999, published to Chappell et al[2]. Chappell et al[1,2] teach a polynucleotide sequence (SEQ ID NO: 21) encoding a monoterpene synthase that shows 52.7% best local similarity to the polynucleotide of

SEQ ID NO: 1. The instant claim neither recites the percentage of sequence homology to the polynucleotide of SEQ ID NO: 1 nor the function/specificity of the encoded protein. Furthermore, claim 2 does not recite the stringency of the hybridization procedure. Therefore under hybridization conditions at low temperature and under mild wash conditions (high salt and low temperature) the polynucleotides disclosed in US 6,559,2971 or US 6,468,772 (Chappell et al[1,2]) can hybridize with SEQ ID NO: 21. Thus SEQ ID NO: 21 anticipates the polynucleotide of SEQ ID NO: 1 or complement of SEQ ID NO: 1 in the instant application. Note that in instant claim 2, the claimed polynucleotide does not have to encode a protein with geraniol synthase activity.

Claim 2 is rejected under 35 U.S.C. 102(b) as being anticipated by SEQ ID NO: 1 in US 6,291,745 filed on October 14, 1998 published to EuClaire Meyer et al (see SCORE results). EuClaire Meyer et al teach a polynucleotide sequence encoding a monoterpene synthase that shows 52.7% best local similarity to the polynucleotide encoding the geraniol synthase of SEQ ID NO: 2. The claim neither recites the percentage of sequence homology to the polynucleotide of SEQ ID NO: 1 nor the specificity of the encoded protein. Furthermore, the claim does not recite the stringency of the hybridization procedure. Therefore under low temperature hybridization conditions and mild wash conditions (high salt and low temperature) this polynucleotide can hybridize with SEQ ID NO: 1.Thus SEQ ID NO: 1 in US 6,291,745 anticipates claim 2 in the instant application. Note that in instant claim 2, the claimed polynucleotide does not have to encode a protein with geraniol synthase activity.

Conclusion: Claim 3 is allowable if written independently.

Relevant publications: Monoterpene biosynthesis in lemon (Citrus limon) cDNA isolation and functional analysis of four monoterpene synthases. Luker et al. Eur. J. Biochem. 269, 3160-3171 (2002).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAGNEW H. GEBREYESUS whose telephone number is (571)272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kagnew H Gebreyesus/
Examiner, Art Unit 1656
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